201-14216

"Alan J. Olson" <OlsonAJ@Ferro.com> on 12/30/2002 06:26:35 PM

To: Rtk Chem/DC/USEPA/US@EPA, oppt.ncic@epamail.epa.gov
cc:

Subject: HPV Filing

Attached is the HPV Filing for Isodecyl Diphenyl Phosphate, CAS 29761-21-5.

Alan J. Olson
Director of Technology
Ferro Corp.

IDP HVP cl 123002.doc IDPHPVtestplan 123002.doc

December 30, 2002
Via email and FedEx

Mr. Oscar Hernandez
Director, Risk Assessment Division (7403M)
U. S. Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460

Attn: Chemical Right-To-Known Program
Re: HPV Challange
Isodecyl Diphenyl Phosphate
CAS Registry Number 29761-21-5

Dear Mr. Hernandez:

As part of Ferro Corporation's commitment under EPA's High Production Volume (HPV) Challenge Program, Ferro is pleased to submit its proposed testing approach for Isodecyl Diphenyl Phosphate. This submission consists of this cover letter, a Test Plan, and robust summaries for the existing studies available on Isodecyl Diphenyl Phosphate.

Ferro understands that this Test Plan will be posted on the Internet and subject to a 120-day comment period. Ferro further understands that all comments by EPA or received by EPA will be forwarded to Ferro for consideration. In the event that additional information on existing studies of Isodecyl Diphenyl Phosphate
becomes available to Ferro during the 120-day comment period, Ferro may wish to amend its submission.

This submission is also being sent electronically to the following e-mail addresses:

oppt.ncic@epa.gov
chem.rtk@epa.gov.

Thank you for your cooperation in this matter. If EPA requires any additional information about this submission, please contact me at 216-750-6696 or olsona@ferro.com.

Sincerely,

Alan J. Olson, P.E.
Director of Technology

201-14216A

U.S. EPA HIGH PRODUCTION VOLUME CHEMICAL VOLUNTARY TESTING PROGRAM

TEST PLAN

ISODECYL DIPHENYL PHOSPHATE

Submitted by:

FERRO CORPORATION
CLEVELAND, OHIO

December 2002

INTRODUCTION

Isodecyl diphenyl phosphate, CAS Registry Number 29761-21-5, is a flame retardant for most commercial resins including polyvinyl chloride and its copolymers, polyvinyl acetate and acrylics. Isodecyl diphenyl phosphate is a clear, odorless liquid with the following physical properties:

Vapor pressure 0.09 kPa @ 28° C
Volatility 1.6% w/w EPA method 24
Viscosity 21.9 mPa @ 25°C
Solubility 0.75 mg/L @ 25°C.

TEST PLAN RATIONALE

At this time, information available on the environmental effects, ecotoxicity and some health effects of isodecyl diphenyl phosphate cannot be documented or is judged to be not reliable according to the standards specified by Klimisch (Regulatory Toxicology and Pharmacology, 25, 1-5, 1997) or the EPA High Production Volume Challenge Program Guidelines for Determining the Adequacy of Existing Data (http://www.epa.gov/chemrtk/datadfin.htm). The exceptions to this are a well-conducted and reported 90-day repeated dose oral toxicity study in rats and an *in vitro* mutation study conducted in mouse lymphoma cells. Summaries of those studies are included as Appendix 1 to this submission. Accordingly, Ferro Corporation commits to generating data, listed in Table 1, necessary to meet address HPV Endpoints. Since an adequate 90-day repeat-dose oral toxicity study in rats has been completed for isodecyl diphenyl phosphate which established an effect level for the test compound and identified target organs for toxicity, no further repeat-dose testing is necessary. Furthermore, since the 90-day study included gross and microscopic examinations of reproductive tissues from male and female animals, and no compound-related adverse effect was produced in any reproductive organ including the testes, developmental toxicity testing is proposed to meet the HPV requirements for reproductive/developmental toxicity endpoints.

Because mammalian cell (L5178Y mouse lymphoma cells) testing for genetic toxicity has shown isodecyl diphenyl phosphate to be cytotoxic but not genotoxic or mutagenic, Ferro proposes no additional gene mutation toxicity testing for this compound. Given the degree of cytotoxicity observed in mammalian cells exposed to isodecyl diphenyl phosphate, bioavailability is not an issue and it is therefore unlikely that an Ames test would add any meaningful information to what exists insofar as gene mutation. Ferro proposed to conduct an *in vitro* chromosome aberration test to complete the genetic toxicity portion of the SIDS HPV screen.

Ferro Corporation is committed to providing EPA with reliable data necessary to complete the SIDS screening matrix for the HPV voluntary challenge; however, Ferro

Corporation is also committed to judicious use of research animal resources. To this end Ferro Corporation will continue to attempt to obtain adequate documentation on existing studies of isodecyl diphenyl phosphate. To the extent that this documentation becomes available to Ferro, the HPV Test Plan submitted herein may be altered to reflect reliance on existing studies.

TEST PLAN: ISODECYL DIPHENYL PHOSPHATE

Table 1 lists the HPV testing planned by Ferro Corporation for isodecyl diphenyl phosphate.

Table 1: ISODECYL DIPHENYL PHOSPHATE HPV TEST PLAN

HPV DATA ENDPOINT	PROPOSED DATA DEVELOPMENT METHOD
1. CHEMISTRY	
Melting Point	OECD Test Guideline 102
Boiling Point	OECD Test Guideline 103
Vapor Pressure	OECD Test Guideline 104
Water Solubility	OECD Test Guideline 105
Partition Co-Efficient	OECD Test Guideline 107
2. ENVIRON-MENTAL FATE	
Photodegradation	Estimate/model
Hydrolysis (Stability in Water)	OECD Test Guideline 111
Biodegradation	OECD Test Guideline 301
Fugacity	Fugacity Level III Modeling
3. HEALTH EFFECTS	
Acute Toxicity	"Up and Down Method" for Acute Oral Toxicity: OECD Health Effects Test Guideline 425 possibly supplemented by *in vitro* testing for dose-range finding
Repeat Dose Toxicity	Adequate repeat-dose study exists; no additional systemic toxicity testing planned.
Repro-Develop. Toxicity	Developmental toxicity study planned: OECD Health Effects Test Guideline 414
Genetic Toxicity	*In vitro* mammalian cell mutation study exists; no additional gene mutation testing planned. *In vitro* Chromosome Aberration Study planned (OECD 473)
4. ECOTOXICITY	
Fish	Acute Toxicity to Fish: OECD Test Guideline 203
Daphnia	Acute Toxicity to Aquatic Invertebrates: OECD Test Guideline 202
Algae	Acute Toxicity to Aquatic Plants (Algae): OECD Test Guideline 201

APPENDIX 1

ROBUST SUMMARY OF GENETIC TOXICITY AND REPEATED DOSE MAMMALIAN TOXICITY TESTING COMPLETED ON ISODECYL DIPHENYL PHOSPHATE

GENETIC TOXICITY

Test material:	Isodecyl diphenyl phosphate (Lot QH-28641)
Type:	*In vitro* mammalian cell mutation
Cell type:	Fischer mouse lymphoma L5178Y derived
Metabolic activation:	Male F-344 rat liver 9000 x G supernatant, Arochlor 1254 induced Assay run with and without activation
Solubility, cytotoxicity determination:	Solubility and toxicity were determined with 4-hour incubation followed by 24-hr expression times in at least 4 dose levels bracketing the concentrations used in definitive testing.
Number of concentrations evaluated:	Positive control, negative control, vehicle control, 5 test concentrations with and without activation
Results:	No evidence for mutagenic activity in the presence or absence of exogenous metabolic activation. Cytotoxicity was produced in the highest concentrations of isodecyl diphenyl phosphate tested with activation.
Reliability:	Reliable
GLP:	Work conducted prior to inception of GLP regulations
Reference:	Litton Bionetics Inc. report 20989, "Mutagenicity Evaluation of S-148 BO-78-85 in the Mouse Lymphoma Forwatrd Mutation Assay" Kensington, MD., August, 1978. D. Matheson, Ph.D., Author.

REPEAT DOSE MAMMALIAN TOXICITY

Oral Toxicity

Test material:	Isodecyl diphenyl phosphate (Lot DC 5A83) 98.4% purity)
Type:	Repeat-dose oral – dietary admixture
Species:	Rat
Strain:	Sprague-Dawley
Sex:	Female and male
Number of animals per dose level:	30, weight range: males 106-143 at study initiation females: 104-133 at study imitiation
Number of dose levels:	Three plus untreated control 140 ppm in diet 1400 ppm in diet 7000 ppm in diet
Administration:	Daily for 90 days
Observations:	Clinical observation Food consumption Body weight Mortality Clinical pathology at mid-study and termination hematology serum chemistry urinalysis Gross and microscopic pathology Organ weights Electron microscopy Analysis of test material and dietary mixtures
Results:	Survival was unaffected by treatment. Dose-related male and female reduced body weight gain (slightly >10% in high dose groups) and reduced food consumption. Lymphocytopenia, decreased red cell indices, increased gamma-GT, as well as other indicators of liver cytotoxicity and/or function, hepatocellular hypertrophy and hyperplasia. No treatment-related changes in any organ or tissue

except liver.

Reliability: Reliable

GLP: Work conducted prior to inception of GLP regulations

Reference: Monsanto Company Environmental Health Laboratory Report number 820160, "Subchronic Study of Santicizer 148 Plasticizer Administered in the Diet to Albino Rats" St. Louis, MO., February, 1986, M. W. Naylor, Study Director